disorder (anxiety disorder); pica, hyperphagia, and delusional anorexia (schizophrenia); hyperphagia and bulimia nervosa (borderline personality disorder); anorexia nervosa (Tourette's disorder); hyperphagia, pica, and rumination (mental retardation); hyperphagia (atypical depression); and severe appetite decrease and rumination (melancholia). In depressive states, the degree of the eating disturbance may be related to the severity of the depressive disorder. In anxiety disorder, the degree of anorexia is more severe in association with depression.

To arrive at a diagnosis, it is important to distinguish between eating disturbances associated with primary psychiatric disorders and the comorbid occurrence of a primary eating disorder (anorexia nervosa and bulimia nervosa) and major psychiatric disorders. This distinction is not always clinically apparent and awaits clarification by future research.

Anorexia nervosa and bulimia nervosa are characterized by considerable self-regulatory psychopathology with profound disturbances in self-representation, self-esteem, and self-stability. There is often a relentless drive toward thinness and reactive counterweight behaviors (self-induced regurgitation, laxative abuse, and exaggerated exercise pattern) in the context of a cognitive preoccupation with food selection, body experience, and weight. Secondary restrictive and hyperphagic eating disturbances seen in major psychiatric disorders are often initially less evident than the more dramatic primary signs of profound mood changes, psychosis, and suicidal behavior.

Eating disorders are not merely "variants" of an affective disorder. A spectrum of clinical features from mild dysthymia to major depression may be associated with a wide range of disturbed eating behavior. A recent positron emission tomographic study (glucose brain metabolic function) found considerable differentiation of cerebral metabolic patterns between women with bulimia nervosa or a depressive disorder and a normal control group. Several lines of research have noted a more extensive eating disturbance (both anhedonic restriction and hyperphagia) correlated with the severity of both the formal eating disorder and the associated primary psychiatric disorder. The most frequent comorbid disorders associated with anorexia nervosa and bulimia nervosa are affective disorder, obsessive-compulsive disorder (17% lifetime incidence of eating disorders), substance abuse, and posttraumatic stress disorder (sexual abuse and victimization). A more detailed understanding of the genetics, clinical manifestations, and complications of comorbidity in the eating disorders may lead to more effective therapeutic interventions in heretofore treatment-resistant patients.

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Nocturnal Enuresis

NOCTURNAL ENURESIS is often considered a result of psychological conflict. Unconscious sexual fears, passivity, exhibitionistic traits, hate for the opposite sex, effeminacy, and castration fears have been mentioned as some psychological causes. Parental inconsistency, punitive or lax toilet training, maternal anxieties, or paternal aloofness have also been implicated. Many pediatricians still send enuretic children to child psychiatrists for therapy once organic causes have been ruled out. Psychotherapy, however, has not been shown to resolve bed-wetting except for the expected spontaneous cure rate.

Bed-wetting shows a high spontaneous cure rate; it occurs in a third of children at age 4, drops to 10% at age 6, and decreases by 15% per year thereafter.

Two major types of bed-wetting can be distinguished. Primary enuresis accounts for 80% of patients who wet their beds. The main causes are physiologic variations of functional bladder capacity, bladder sphincter muscle control, or sleep disturbance. A strong genetic factor is often apparent. In secondary enuresis, bladder control had been gained but then was lost—mostly due to regression in response to a stressful event. In some instances, secondary emotional problems develop. Most enuretic children, however, do not show primary or even secondary emotional disturbance.

New, developmentally based approaches have dramatically changed the assessment, treatment, and severity of the psychological consequences of enuresis. Treatment options need to take spontaneous resolution into account.

Education is one available method. To relieve unnecessary feelings of guilt and blame, it is important to help the parents and the child understand that bed-wetting is a developmental rather than an emotional problem. For children younger than 6, reassuring parents by stressing the self-limited nature of the problem for most children may be sufficient. For children older than 6, bed-wetting can be embarrassing; therefore, most can easily be counseled to become active participants in their treatment. Restricting fluids and urinating before bedtime may increase the number of dry nights and give a motivating sense of success. Parental management of enuresis should be nonpunitive; dry nights should be praised; wet nights ("accidents") should be handled matter-of-factly with agreements on who should clean the sheets and pajamas. Parent-child education alone leads to noticeable improvement in 70% of enuretic children. Bladder stretching and urine stream interruption exercises have a cure rate of about 35%. Bed-wetting alarms are most effective in children older than 8 years and show a cure rate of 70%. They should be used until three weeks of continuous dryness are achieved.

The use of medications in the treatment of enuresis is controversial. Only imipramine hydrochloride, a tricyclic antidepressant, has been extensively studied. Low dosages (50 to 75 mg at bedtime) are required; while notable improvement has occurred in half of the treated children, relapse rates after the drug is discontinued are high, and a cure rate of only 25% can be expected. Because of the high toxicity of antidepressant agents and their limited effectiveness, their use is rarely indicated.

More success with no recognizable adverse effects has recently been described with the nightly intranasal use of 20 to 40 μg of desmopressin acetate, an antidiuretic agent. Des-

mopressin use causes immediate improvement in 70% of enuretic children; relapse rates are lower than with the use of imipramine but higher than with bed-wetting alarms.

Secondary regressive enuresis responds best to crisis intervention to help the child and family cope with the identified stress that triggered the bed-wetting episode. Counseling as to the transient nature of the bed-wetting problem may prevent a more serious maladaptive response.

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Treatment-Resistant Depression

THE BEST ESTIMATE IS THAT about 20% of depressed patients do not respond adequately to treatment. As the debilitating effects of depressive disorders on patients and their families become more apparent, it is important to develop effective pharmacologic strategies for patients whose depressions are resistant to treatment. Physicians have been hampered, however, by a lack of consensus in defining treatment resistance. It is clear that treatment intolerance—the inability to tolerate one or more antidepressant agents in sufficient doses to effect a response—needs to be distinguished from true treatment resistance. Beyond that, whether treatment resistance should be defined by a level of symptoms for a certain period of time or by a failure to respond to a number (but how many?) of antidepressant drugs at specified doses or plasma concentrations is still debated. Similarly, some authors have suggested that patients not be called treatment resistant until they have had a trial of electroconvulsive therapy, and others see electroconvulsive therapy as a strategy for patients already defined as treatment resistant.

Among patient characteristics that may predict treatment resistance, the presence of other concomitant disorders is the most important. Patients who both are depressed and have drug or alcohol abuse, severe personality disorders, or active significant medical illness have lower response rates to antidepressant treatments.

Although there are a variety of creative pharmacologic strategies for treating refractory depressions, the most important recommendations involve using the more common treatments correctly. As an example, patients should not be considered treatment resistant until they have had a trial of one tricyclic antidepressant at a dosage level of imipramine hydrochloride, 300 mg per day, or its equivalent for at least six weeks. With some antidepressants, determining trough serum concentrations of the tricyclic prescribed (the blood specimen to be drawn in the morning after nighttime dosing) and adjusting the dose according to the serum level will further enhance the adequacy of treatment. A substantial number of patients referred to as treatment resistant will not meet even this first criterion because many clinicians stop an antidepressant medication after three or four weeks of treatment, a strategy that will decrease response rates by as much as 25%.

Patients who have not responded to an adequate trial of one tricyclic antidepressant should be treated using any one (or all four, if no response is seen) of the following strategies: adjunctive medications such as lithium carbonate added to the tricyclic regimen; switch to a cyclic antidepressant of a different class, such as fluoxetine; switch to a monoamine oxidase inhibitor antidepressant (this is probably the most underused effective strategy); or electroconvulsive therapy (for more severely depressed patients). For those patients treated with fluoxetine first, the tricyclic antidepressant would simply be substituted in its place.

Only if these basic strategies fail should the more unusual therapies, such as stimulants, combined tricyclic and monoamine oxidase inhibitor antidepressants, combined fluoxetine and tricyclics, or the anticonvulsants be tried.

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Antidepressant Treatment in Patients With Heart Disease

THE GROWING RECOGNITION that substantial medical morbidity and mortality are associated with depression has led clinicians to treat depression in patients with coexisting serious medical disorders if it can be done safely. Because cardiac toxicity of antidepressant treatment may be the most serious concern for clinicians, it is important to review recent advances that have increased the safety of treating depression in patients with heart disease.

The most serious complication requiring caution is a conduction disturbance, especially left bundle branch block or hemiblock. Tricyclic antidepressant agents have a quinidine-like (class IA antiarrhythmic) effect, slowing conduction and potentially causing complete heart block. Indeed, complete heart block and arrhythmias are the probable causes of death in tricyclic overdose. The use of tricyclic antidepressants is contraindicated in the presence of left bundle branch block or hemiblock but not right bundle branch block because of the latter's small size. They may have additive toxicity with other class IA antiarrhythmic agents including quinidine, procainamide hydrochloride, and disopyramide phosphate. An additional problem is that the slowed metabolism of tricyclic antidepressants can exacerbate side effects including orthostatic hypotension. Trazodone may be given to patients with conduction disturbance with careful monitoring. The same may be true for fluoxetine, buproprion hydrochloride, monoamine oxidase inhibitors, and psychostimulants (methylphenidate and others).

The use of tricyclic antidepressants is generally safe in patients with ventricular ectopy because of their quinidine-like antiarrhythmic actions. In contrast, trazodone may exacerbate preexisting ventricular arrhythmias for unknown reasons. Until further research is done on this problem, trazodone should generally not be used in this context.

Antidepressant therapy is generally safe in patients with diminished cardiac contractility, as these medications do not appear to have a negative inotropic effect. Patients with ejec-